Schizophrenia and Dementia with Behavioral Symptoms

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Case Presentation

An 82-year old African-American woman, DH, was admitted to an assisted living (AL) facility in April. Her admitting diagnoses were schizophrenia, Alzheimer's disease (AD) with some behavioral disturbances, hypertension, and anemia related to chronic renal insufficiency. DH is recovering from a left hip fracture, but ambulates quite well. She requires minimal assistance with her activities of daily living (ADLs). Although DH has memory problems, her vision and hearing are good for her age. She has occasional incontinence. DH is 5' 1", weighs 130 lbs, has no known drug allergies, and her family relatives are unknown. A nursing note several days after admission states that DH is reluctant to take her medications and that her mental function varies throughout the day.

DH's medications are listed in Table 1, and pertinent lab values, ordered at admission by her new physician, are listed in Table 2.

On May 12, the provider pharmacist was in the facility for a staff education presentation. The pharmacist reviewed DH's chart, maintained in the medication storage room, spoke with the facility nurse and resident care assistants, and observed DH in the dining room. The pharmacist was investigating the ziprasidone discontinuation and the regular use of as-needed (prn) lorazepam during early May (Table 3).

Table 1.
DH's Medications

Donepezil, 5 mg PO daily

Ferrous sulfate, 325 mg PO daily

Ziprasidone, 80 mg PO every morning and 40 mg PO every evening (discontinued April 27)

Multiple vitamin with minerals, PO every day

Amlodipine, 10 mg PO daily

Lorazepam, 1 mg PO (1-2 tablets every 4 hours prn for increased agitation)

Table 2.
Laboratory Findings

Test	Result	Reference value
Sodium	126	135–147 mEq/L
Potassium	4.8	3.5–5.0 mEq/L
Chloride	105	95–110 mEq/L
BUN	30	8–25 mg/dL
Serum Creatinine	1.7	0.5–1.7 mg/dL
Glucose	120	65–115 mg/dL
Calcium	9.0	8.6–10.3 mg/dL
Hemoglobin	8.5	12–15 g/dL
Hematocrit	27	33%–43%

Treating Schizophrenia

Schizophrenia is a chronic psychiatric disorder with multiple symptoms. According to the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition, (DSM-IV) a patient with schizophrenia must have 2 or more of the following symptoms present regularly during a 1-month period: delusions, hallucinations, disorganized speech, grossly disorganized or catatonic behavior, and negative symptoms such as affective flattening or poverty of speech.[1] Patients will also exhibit impaired functioning, such as poor self-care.[1] Patients with schizophrenia often also have cognitive dysfunction, leading to memory and attention problems, and mood disturbances (eg, anxiety, agitation, and hostility).[1,2] Patients who are untreated, or who discontinue their medications, develop multiple problems.[2]

Therapy for geriatric patients with schizophrenia focuses on controlling behavior and relieving symptoms while avoiding undue side effects. Preferred agents are the atypical antipsychotics.[2-10] Geriatric patients with schizophrenia frequently suffer from delusions and auditory hallucinations.[9] Unlike psychosis associated with AD, which may remit as the AD progresses, schizophrenia rarely remits, although the severity of symptoms may lessen.[9]

Atypical antipsychotics treat the positive and negative symptoms of schizophrenia and may also alleviate mood disturbances and cognitive symptoms.[2,3] Atypical antipsychotics are associated with a lower incidence of extrapyramidal symptoms (EPS) than typical antipsychotics.[6] How-

ever, geriatric patients treated with atypical agents have an increased incidence of EPS compared with younger patients.[6,9] Atypical antipsychotics are associated with sedation, orthostatic hypotension, and metabolic adverse effects, such as weight gain, increased blood glucose, dyslipidemia, and increased blood pressure.[3-10] Safety and tolerability among agents varies, and a low dose of one agent is usually started in geriatric patients. Initial choices may include quetiapine, olanzapine, risperidone, aripiprazole, or ziprasidone.[3] If the patient has an inadequate response, a trial with a different atypical agent is indicated.

Clozapine is only used in geriatric patients with schizophrenia who have failed trials with multiple atypical agents.[3,4] Recommended doses of atypical antipsychotics for geriatric schizophrenic patients are approximately 50% of doses given to younger patients because the disease stabilizes over time, geriatric patients have comorbidities, and side effects are more likely to occur in these patients.[9]

Treating Dementia and Behavioral Disturbances

There are many classifications of dementia; AD is the most common cause of dementia.[7] Current treatments for AD are not curative nor are they known to directly reverse the process of the disorder, so the primary treatment goals are to maintain patient functional and cognitive abilities for as long as possible.[7] Secondary goals are to treat the psychiatric and behavioral problems that arise as a result of the disease.

The only medications approved by the Food and Drug Administration (FDA) for AD are the cholinesterase inhibitors and the N-methyl-D-aspartate antagonist, memantine. These medications slow the progression of AD. Donepezil, the cholinesterase inhibitor DH is taking, has an initial dose of 5 mg at bedtime for 4 to 6 weeks.[8] The dose should then be titrated to 10 mg at bedtime, if tolerated. Dosage titrations reduce the incidence of gastrointestinal side effects, namely nausea and diarrhea. Memantine is FDA approved for moderate to severe AD at a maintenance dose of 10 mg twice daily.[7,8] In clinical practice, memantine may be initiated when the patient has mild to moderate AD.

Atypical antipsychotic agents may be used for the temporary management of psychosis, severe agitation, or very disruptive behavior in AD patients.[6-10] As patients progress in their AD, approximately 20% to 40% experience psychoses, delusions, or hallucinations at some point in the disease process, which can lead to agitation and anxiety.[6] Atypical antipsychotics are approved for treatment of schizophrenia; however, they are not FDA approved for AD behavioral disturbances unless the patient has psychotic features.[6] Several decades ago, the typical antipsychotics were overused in geriatric individuals as chemical restraints, prompting regulations concerning psychoactive medication use in long-term care facilities.

Physicians use any psychoactive agent with caution in all older individuals, regardless of their residence. Atypical antipsychotics are only FDA approved for psychotic features with dementia, and their use is associated with the side effects previously discussed.[3-10] For AD behavioral disturbances, behavior modification is the preferred therapy. Antidepressants and acetylcholinesterase inhibitors may be helpful in controlling behavioral symptoms of AD and are preferred as medication therapy over antipsychotics.[7,10] Selective serotonin reuptake inhibitors are prescribed to many AD patients to improve mood and decrease hostility.[7] When antipsychotic use is unavoidable, practitioners should consider risks and benefits, use the lowest effective dose, document symptoms, and periodically reevaluate usage.[6,9,10]

DH's long-standing schizophrenia warrants antipsychotic use. There is an order for ziprasidone. The initial dose of ziprasidone for schizophrenia in geriatric patients is 20 mg twice daily, with titration upward based on response, to generally no more than 80 mg twice daily.[8] Because metabolic disturbances of weight gain, poor glucose control, dyslipidemia, and even hypertension can develop or worsen with chronic use of atypi-

THOUGHTS ON AGING

People like you and I, though mortal of course like everyone else, do not grow old no matter how long we live...[We] never cease to stand like curious children before the great mystery into which we were born.

– Albert Einstein, in a letter to Otto Juliusburger

Table 3.
Lorazepam PRN Doses Taken in May

Agitation

Date	# doses
1	0
2	0
3	0
4	0
5	0
6	2
7	1
8	1
9	2
10	1
11	2

cal antipsychotics, DH's weight, blood pressure, blood glucose, and serum lipids should be monitored.[3,4,6] Laboratory monitoring may be done less frequently in an AD patient, depending on family wishes and the judgment of the healthcare provider. Atypical antipsychotics also cause varying degrees of sedation, which can increase the risk of falls, so other sedative agents should be avoided, if possible.[9]

Benzodiazepine antianxiety medications (ie, lorazepam) may be used on a short-term basis to treat agitation, but these drugs are not recommended for routine use in geriatric patients because of their side effect profile and potential for tolerance.[11] The intramuscular and oral formulations of lorazepam are not FDA indicated for treatment of agitation associated with schizophrenia, but the oral form of lorazepam is indicated for anxiety or insomnia associated with anxiety.[8] DH has an order for oral lorazepam for increased agitation, and in May she took numerous doses (Table 3).

Comments and Suggestions

When DH was admitted to the AL facility in April, she had orders for lorazepam prn and scheduled ziprasidone. By May the ziprasidone was discontinued because DH was refusing the medication at times. No adverse effects from ziprasidone were noticed by the staff or noted in the chart. Abrupt withdrawal of antipsychotics can result in withdrawal symptoms of restlessness, insomnia, and nightmares, which DH could have experienced.[3] For the past 2 weeks DH has been resisting care and was twice verbally abusive to the resident care assistants, but the staff did not categorize DH as acutely agitated. It would be best to avoid the continued regular use of the prn lorazepam. Regular use of lorazepam places DH at increased risk of falls and worsening confusion, and it does not effectively treat schizophrenia.[12]

The pharmacist and facility nurse discussed DH's case, and the nurse contacted the physician with a request to consider a trial with another atypical antipsychotic, such as olanzapine, quetiapine, risperidone, or aripiprazole. Olanzapine is only administered once a day and is available in an orally disintegrating tablet, which could be helpful with DH's nonadherence.[5,8] Risperidone is also available as an orally disintegrating tablet, but is normally given twice a day for schizophrenia.[8]

For her AD, DH is taking donepezil 5 mg every day. The staff indicated that DH has been taking donepezil for more than 4 to 6 weeks with no reported adverse effects. The physician increased the dose to 10 mg once daily, the recommended maintenance dose.

In the next issues of *ALC*, DH's hypertension, renal insufficiency, and anemia will be discussed. ALC

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